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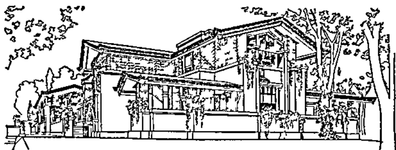
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HEMODYNAMICS IN FAILURE OF THE CIRCULATION

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PREFACE

VIEWPOINTS concerning the pathologic physiology of failure of the circulation have undergone a radical change within the past ten years This article is written primarily for three classes of readers 1) those considering the subject of failure of the circulation for the first time e g medical students 2) those who have not had opportunity to do systematic reading on the subject during recent years and 3) those who wish to review the subject in the light of basic physiologic facts Others who are quite familiar with the literature on failure of the circulation perhaps will be interested to see which of various controversial interpretations we have chosen to support We began the study by collecting literature containing pertinent *measurements* in patients with failure of the circulation After studying the cardiovascular patterns in the various types of failure we were impressed by the necessity of subdividing conditions associated with chronic venous congestion into two categories 1) chronic congestive heart failure and 2) chronic venous congestion without failure The latter group includes the conditions in which there is a higher than normal cardiac output and no evidence of cardiac weakness When this initial subdivision is used few inconsistencies or paradoxes are encountered

We have presented systematically the mechanisms by means of which left ventricular failure may lead to an elevation of both pulmonary and systemic venous pressure The prominent role of the kidney in various types of failure is described The reasons for the inconsistence of the relationship between systemic venous pressure and the status of the right ventricle are made clear We have

not used the terms backward failure or forward fail ure because these terms have been used in many senses so that they no longer serve as an aid to clarification of the mechanisms involved We do not use the term back pres sure since in a closed circuit where blood is being pumped forward with greater or lesser speed the source of pressure is always upstream

The bibliography includes not only references but also other papers basic to the development of present knowl edge of the subject

W B Y
A R H

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HEMODYNAMICS IN FAILURE OF THE CIRCULATION

INTRODUCTION

MAINTENANCE of the cardiac output at a level within the normal range depends upon filling of the atria and hence of the ventricles under an adequate head of *venous pressure*, and upon a normal *ventricular response to filling* Since the circulation depends upon these two major factors there are two quite different types of failure of the circulation

In failure of the venous return the heart is capable of responding normally to the venous pressure but blood is not reaching the heart in sufficient amounts This type of circulatory failure usually is caused either by a severe decrease in blood volume or by a loss of arteriolar tonus in the systemic circuit or by a combination of these two factors

A subnormal output of the ventricle at a given venous pressure level is caused by various types of conditions which will be classified later The essential feature common to such conditions is a defect in or interference with the transport of blood This defect or interference may be in the right heart pulmonary circuit left heart or systemic arteries Characteristically the pressure in the veins of the systemic or pulmonary circuit or both becomes elevated

The failure initiated by insufficient return of blood to the heart is commonly referred to as *peripheral circulatory failure*, while *heart failure* strictly speaking refers to the failure of the circulation initiated by deficient transport of blood by the heart When heart failure occurs suddenly as in myocardial infarction it is called acute heart failure and when it develops more or less gradually as in patients having certain valvular lesions it is called chronic heart

failure The term *decompensation* is synonymous with failure

Well established chronic heart failure is characterized by congestion [1] of veins cardiac [2] dilatation and dependant [3] edema However there is a group of conditions in which these findings are present but in which there is no impairment in the transfer of blood anywhere in the cardiovascular system The latter syndrome ordinarily is called heart failure also but in this paper it will be called *chronic venous congestion without failure* It is considered in the final section The following classification of types of failure of the circulation will be used as a basis for discussing hemodynamics

- I Failure of the venous return
  - A Inadequate blood volume
  - B Loss of arteriolar tonus
  - C Obstruction of venous drainage
- II Failure of the heart
  - A Acute combined right and left ventricular failure
  - B Acute failure of the left ventricle
  - C Chronic failure of the left ventricle
  - D Right ventricular failure in the presence of left ventricular failure
  - E Acute failure of the right ventricle
  - F Chronic failure of the right ventricle
  - G True chronic congestive heart failure

Before discussing failure of the circulation certain basic principles concerning blood pressure blood flow and the distribution of blood in the cardiovascular system will be considered

— 1 —

BASIC PHYSIOLOGICAL PRINCIPLES

RELATIONSHIP BETWEEN VENTRICULAR FILLING AND STRENGTH OF VENTRICULAR CONTRACTION

IN A closed elastic system changes in volume and changes in pressure are inseparable An increase in volume is accompanied by an increase in pres sure the degree of rise in pressure being greater the less distensible the system The rise in pressure with incre ments of volume in various parts of the cardiovascular system within the range observed in normal and path ologic physiology is not linear Curves for a section of a large *vein and a section of a large artery are illustrated* in Figure 1 At the lower volumes introduction of a given volume causes a lesser rise in pressure than that produced by the same increment in volume at a higher volume level This is equivalent to saying that a given rise in volume in a relatively unfilled portion of the cardiovascular tree will result in a slight increase in pressure while the same degree of increase in volume in a filled portion of the cardiovascu lar tree will result in a considerable rise in pressure

Several decades ago Starling and associates studied the relationship between ventricular filling (and consequently of diastolic ventricular size) and the strength of ventricular contraction Starling s law of the heart based on these data states that the strength of ventricular contraction increases with increasing diastolic ventricular size up to a certain optimal value beyond which an increase in di astolic volume is associated with a decreased strength of

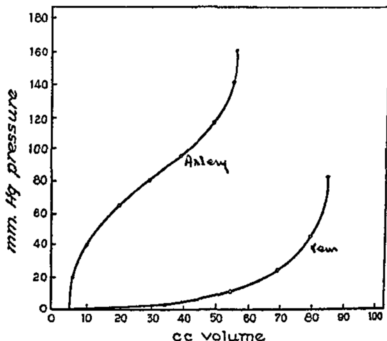


FIGURE 1 *Relationship between intravascular pressure and volume* The upper curve represents an isolated segment of a large artery the lower curve a segment of a large vein A given volume of fluid introduced into a collapsed vein will cause a slight pressure increase while the same vol ume introduced into a distended vein will cause a marked increase in pressure Particular attention should be given to changes within the physiologic range of pressure in each type of vessel (After Best & Taylor *Physiological Basis of Medical Practice* 4th Ed Page 123)

contraction At a given heart rate diastolic heart size is determined largely by the head of pressure in the great veins and atria Any increase in venous pressure within the normal range in a Starling heart lung preparation in which reflex pathways are eliminated will cause increased *ventricular filling increased strength of ventricular con* traction and increased stroke volume against constant mechanical conditions on the arterial side Heart rate re

mains virtually unchanged hence cardiac output is increased in proportion to the increased stroke volume However when the venous pressure is already quite elevated a further increase in pressure as illustrated in Figure 2 results in decreased stroke volume and a corresponding decrease in cardiac output

In brief there is an increased cardiac output through increased filling and increased strength of ventricular contraction as the venous pressure is increased up to a certain critical level beyond which a rise in venous pressure causes a decrease in cardiac output

Throughout this paper it is accepted as a fact that any

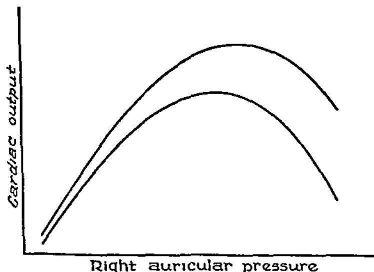


FIGURE 2 *Changes in cardiac output in response to changes in right auricular pressure in the absence of neural or humoral influences for the normal heart (above) and for the weakened heart (below)* This illustrates that for a given filling pressure the output of the weakened heart is less than for the normal on the other hand the weakened heart may attain an output in the normal range in the presence of a higher than normal venous pressure

alteration in venous pressure *per se* influences output of either the normal or the failing heart However there are other influences working simultaneously in the same or the opposite direction and cardiac output during a given period is the resultant of these influences It is an unfortunate choice of words to say that Starling s law is not operating when an increased cardiac output is associated with a decreased venous pressure as for example from increased activity of the cardio accelerator nerves In such cases the cardiac output is certainly less than it would be if the venous pressure were maintained in the presence of this degree of cardio-accelerator activity

Starling s law of the heart not only affords a basis for an increased cardiac output in response to increased venous pressure but it also is concerned in the maintenance of cardiac output against an elevated arterial blood pressure In the heart lung preparation as the arterial pressure is elevated the amount of blood remaining in the heart at the end of systole is increased and during diastole the heart fills to a larger size This causes an increased strength of contraction which in this case serves to eject the same volume of blood against the increased resistance Again a critical arterial pressure may be reached beyond which the diastolic ventricular size becomes excessive and against which the ventricle cannot pump so that a fall in cardiac output will result

In summary the relationship between initial length of ventricular muscle and the strength of its contraction is such that within limits 1) an increased venous pressure causes an increase in cardiac output and 2) cardiac output is maintained in the presence of an increased arterial blood pressure

VENOUS PRESSURE AND REFLEX EFFECTS UPON RATE AND STRENGTH OF VENTRICULAR CONTRACTION

In addition to the adjustments of the cardiac output to venous pressure on the basis of changes in diastolic heart size there are reflexes elicited by a rise in venous pressure which also serve to increase output The reflex increase in heart rate under these conditions is known as the atrial or Bainbridge reflex Since the sympathetic pathways provide the efferent limb a reflex increase in the strength of ven tricular contraction probably is involved also The afferent fibers for the reflex are contained in the vagus nerve

Thus in the intact circulation a rise in venous pressure may be expected to cause an increase in cardiac output on the basis of Starling s law of the heart and the Bainbridge reflex A rise in venous pressure can be produced in man by rapid intravenous administration of fluid In most studies this has resulted in an increase in cardiac output in proportion to the rise in venous pressure (3 99 186 200)

REFLEX MECHANISMS COUNTERACTING A CHANGE IN SYSTEMIC ARTERIAL BLOOD PRESSURE

The response of the heart to the *arterial* blood pressure insofar as the response in based on Starling s law is such as to maintain an unchanging output in the presence of a changing arterial pressure Under physiological condi tions and some pathological conditions there are consider able changes in resistance to outflow from the arterial tree due to changes in the state of contraction of the smooth muscle in the arterioles (119) Changes in cardiac output in response to changes in arterial pressure are accom plished largely through the carotid sinus and aortic arch reflexes

Afferent fibers concerned with these reflexes pass from the aortic arch via the vagi bilaterally and from the two carotid sinuses via branches of the glossopharyngeal and vagus nerves On the efferent side the pathways involved are diffuse both the sympathetic and parasympathetic nerves to the heart and blood vessels are utilized These reflexes operate as follows The degree of activation of re-

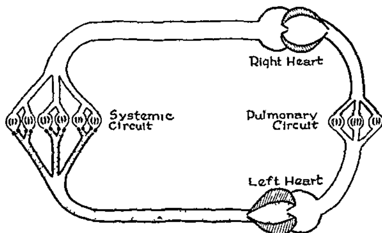


FIGURE 3 *Diagram of the circulatory system* The portion in which the mean pressure exceeds 25 mm of mercury is stippled The mean pressure gradients are shown in Figure 4

ceptors in the carotid sinuses and aortic arch varies with sudden changes in the pressure level A rapid increase in pressure results in an increase in the number of impulses passing from the receptors up the afferent nerves to the medulla oblongata By means of connections in the medulla the number of impulses passing out over the (vagal) cardio-inhibitory nerves is increased while the activity of the cardio accelerator nerves (mainly sympathetic) is decreased At the same time the tonic activity of vasoconstrictor nerves (contained largely in the sympa-

thetic system) is decreased and possibly vasodilator nerves are activated Thus the rise in arterial pressure is counter acted reflexly both by a decreased input of blood into the arterial system and by a decreased resistance to outflow from the arterial tree A fall in blood pressure as seen during hemorrhage has the reverse effects since it is associated with a decrease in the number of impulses initiated in the receptors of the aortic arch and carotid sinuses

COMPARISON OF HEMODYNAMICS IN THE SYSTEMIC AND PULMONARY CIRCUITS

Since normally there is no flow of blood directly from the left side of the heart to the right side the circula tory system may be diagrammed as in Figure 3 Although anatomically there are two circuits when the route of a unit of blood is considered there is one circuit con taining two separate pumps the right heart and the left heart The volume of blood flow per unit of time at any cross section of the system cannot be different from the flow at any other cross section for very long otherwise blood would progressively accumulate at some site in the system Momentary differences in flow in the two circuits do occur under certain conditions and are associated with transfer of blood from one circuit to the other On the other hand during any prolonged period the output of the right ventricle must equal the output of the left ventri cle Since the right ventricle maintains an output equal to the output of the left ventricle and the mean pressure in the pulmonary artery is approximately one sixth the mean pressure in the aorta it is evident that the resistance to flow of blood through the pulmonary circuit is a small fraction of the resistance to flow in the systemic circuit The difference in amount of work done by the two ventri cles is approximately proportional to the difference in re sistance to flow The pressures throughout the two circuits

are shown in Figure 4 which also illustrates that the mean length of the systemic circuit is much greater than that of the pulmonary circuit

The fraction of the total blood volume contained in the pulmonary circuit is small compared to the amount contained in the systemic circuit Figures obtained by various

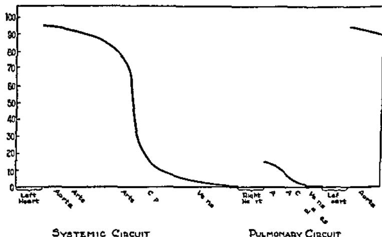


FIGURE 4 *Mean pressure gradients in the systemic and pulmonary circuits* Vertically the pressure scale in mm of mercury is shown Horizontally the relative mean lengths of the two circuits are roughly illustrated This figure should be studied along with Figure 3 to visualize changes in distribution of blood associated with changes in pressure and volume in the systemic arteries

methods indicate that 12 to 20% of the blood volume is contained in the pulmonary circuit Under normal conditions alterations of this fraction i e shift of blood from the systemic circuit to the pulmonary circuit or the reverse is accomplished through alterations in vasoconstrictor tonus in the systemic circuit Vasodilatation allows the blood to pool in the large systemic capillary bed and the volume of blood in the pulmonary vascular bed is propor

tionately decreased Conversely widespread systemic vaso constriction will result in transfer of blood into the pul monary vascular bed and, at the same time cause an in crease in pressure in the pulmonary capillaries Thus the lungs function as an important blood reservoir more or less passively accepting whatever volume is transferred from the systemic circuit There is evidence that the pul monary arterioles like the systemic arterioles are supplied with vasomotor nerves from the autonomic nervous system but the degree of their influence is debatable It is obvious from the relative volumes in the two circuits under normal conditions that a sudden transfer of blood from the sys temic circuit into the pulmonary circuit from any cause could engorge the pulmonary circuit but the amount of blood that could shift from the pulmonary circuit to the systemic circuit would not be sufficient to flood the sys temic circuit

When the blood volume is increased above the normal level (plethora) it is accommodated largely in the capillary beds Experimentally plethora of a degree which alone will not produce pulmonary edema when combined with vasoconstriction will produce pulmonary edema with great rapidity since enough blood will be shifted into the pul monary system from the systemic capillary bed to produce a rise in hydrostatic pressure sufficient to cause transuda tion of fluid into the alveoli

Knowledge of these facts concerning the two circuits is necessary for an understanding of failure of the circula tion Although heart failure frequently involves disturb ances in the flow of blood in certain types of failure and in certain stages of chronic congestive failure the disturb ances in volume and distribution of blood are striking while changes in blood flow are minimal (136)

IMMEDIATE CHANGES INCIDENT TO A DECREASED CARDIAC OUTPUT

The immediate effects of a decrease in cardiac output on arterial pressure and venous pressure have been described by Starling (158) Starr (164) and others who have made use of two-circuit artificial circulation models to illustrate some of the changes which occur Starr recently has used a one-circuit schema (160)

In this laboratory a simple one-circuit model having certain characteristics of the cardiovascular system is used to illustrate the direction of the initial changes in arterial and venous pressure produced by alterations in cardiac output and peripheral resistance The essential features of the model are as follows

1 A motor driven piston pump capable of various rates and various stroke volumes and two check valves to maintain one way flow

2 A closed elastic system Elasticity is obtained on the arterial side by air filled thin rubber tubing attached to an upright side arm which can be closed off by means of a gate valve Elasticity and reservoir function are obtained on the venous side by the use of an air dome of appropriate size

3 Peripheral resistance of any desired degree is obtained by a gate valve

4 Fluid is introduced into the system from a pressure bottle until the volume is such that a positive pressure is produced the pump being at rest Lateral pressure is recorded from the arterial side and from the venous side by means of two manometers

In such a system when either pump output or peripheral resistance is altered the change in venous pressure is in the reverse direction of the change in arterial pressure When blood volume is increased both venous and

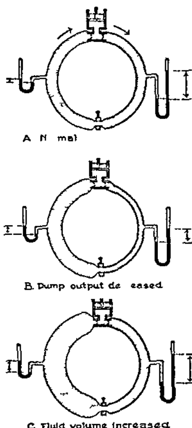


FIGURE 5 *Schema of a one ci cuit circulation mod l designed to illustrate initial changes in pressure and olume on the arterial and venous side produced by altering pump output fluid volume or peripheral resistance* Essential features of the model are described in the text Figure 6 is made from a kymographic record of the pressure changes

A Normal conditions simulated

B Decrease in pump output

C Increase in blood volume

This is the simplest schema to illustrate *initial* changes since no compensation can occur by either neural or humoral influences or by Starling's law The compensatory mechanisms when present do not alter the direction of the initial change but reduce the degree

associated with increased pulsations and negligible mean pressure changes throughout the system The changes in systolic diastolic and pulse pressure with changes in rate stroke volume and peripheral resistance are as produced in the various other circulation models designed to illus trate changes in arterial pressure

The Concept of Mean Systemic Blood Pressure (158) or Static Blood Pressure (9 164) Essential features of any circulation model which is designed to illustrate changes in venous pressure are that the system be closed and that sufficient fluid be introduced so that a positive pres sure is produced throughout the system with the pump at rest That such a relationship exists in the mammalian circulation is indicated in several ways In the first place it can be inferred from the fact that the mean pressure recorded at any point in the system is positive when the heart is beating It is obvious that cessation of heart action would be followed by a fall in pressure and volume in the arteries where the pressure is high and a rise in pressure and volume in the venous system where pressure is low until the pressure throughout the system becomes equal This pressure must be positive unless the contractile ele ments of the vascular bed relax and thus increase the capacity of the system when the heart stops Actually in the intact animal when cardiac output suddenly decreases or ceases the fall in arterial blood pressure elicits a severe contraction of the arterioles and probably there is an in creased venomotor tonus so that the capacity of the cardio-vascular system decreases

In the second place the static pressure can be demon strated experimentally If asystole is produced and main tained by stimulation of the peripheral end of the sec tioned vagus (in an eserinized dog) arterial blood pressure falls and venous pressure rises so that the levels approach each other (80) A similar result is observed if the circula

tion is brought to an abrupt stop by ventricular fibrillation or by cardiac tamponade (184) The static pressure is not high since the veins normally are relatively unfilled and will accommodate the considerable rise in volume with only a moderate rise in pressure Starr has shown that a static pressure is present in patients for some minutes after cardiac arrest (159) The static pressure averaged 7 2 cm in 25 patients who did not have congestion or cardiac abnormality whereas in 10 patients who died in congestive heart failure it averaged 20 7 cm It is considered that the increased level of the static blood pressure under these conditions is related in large part to increased blood volume

The Effects Produced by Decreasing Pump Output In the artificial schema at a given pump output a constant pressure gradient is maintained in the system and there is a constant rate of flow from the arterial side to the venous side Any desired difference between arterial and venous pressure is obtained by adjusting the peripheral resistance a relatively high resistance being required to obtain a wide difference between these two readings When the pump output is decreased either by decrease in rate or stroke volume the rate of outflow from the arterial side does not immediately decrease to the lower level of input into the arterial side Outflow from the arterial side exceeds the pump input for a brief period as the arterial pressure falls off to a lower level The distended arteries serve as the source of energy to promote this transfer of fluid to the venous side Thus when the resistance to outflow is constant the degree of distention of the elastic system that will be maintained depends upon the rate of input into the system For any level of input into the system a given degree of distention is established and output is equal to input

In short when there is a decrease in output of the pump

there is a brief period during which more fluid flows to the venous side than is transferred by the pump from the venous to the arterial side Thus there is a decrease in pressure and volume on the arterial side and an increase in pressure and volume on the venous side until a new equilibrium is established The changes in pressure are illustrated in Figure 6 The extent of the rise in pressure on the

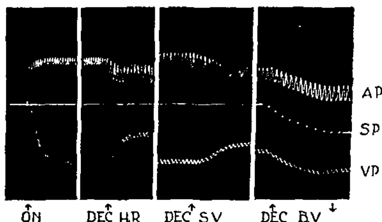


FIGURE 6 *Effects of changes in rate stroke volume and blood volume upon arterial pressure (A P) and venous pressure (V P) in the circulation schema* This figure should be studied in conjunction with Figure 5 The straight line indicates the pressure throughout the system when the pump is at rest This pressure is brought up to any desired level by introducing fluid into the closed elastic system The *first* record illustrates the progressive increase in "arterial pressure and decrease in venous" pressure until an equilibrium is established when the pump starts suddenly at a given output The peripheral resistance is at a relatively high level as in the systemic circuit of the cardiovascular system The *second* record shows the fall in "arterial pressure and rise in venous pressure which occurs when the rate of the pump suddenly is decreased with stroke volume remaining unchanged The *third* record illustrates the similar changes in mean pressures when stroke volume is decreasing with rate remaining constant In the *fourth* record the effects of decreasing the blood volume are illustrated In this case static pressure also falls in proportion to the fall in blood volume

Changes in rate and stroke volume have additive effects when they are both decreased or both increased and effects on the pressures are neutral and when one is increased while the other is decreased.

venous side associated with a decreased pump output de pends 1) upon the extent to which the venous side was filled prior to the decrease in output and 2) upon the distensibility of the venous system The energy for transfer of blood from the arteries to the veins when cardiac output decreases comes from the distended arteries

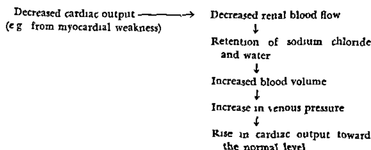
Decreased output of the heart either in the mammalian circulation or in artificial schemas of the type described is accompanied by a redistribution of blood towards the venous side and a rise in venous pressure In the artificial circulation schemas the rise in venous pressure is produced entirely as a direct result of the decreased output In the intact circulation it must be considered that a decreased output *per se* could contribute to the observed rise in venous pressure in the same way that it does in the circula tion models but also as soon as arterial blood pressure is lowered and venous pressure is elevated certain well de fined compensatory mechanisms are immediately brought into action By means of carotid sinus and aortic arch re flexes the fall in arterial blood pressure causes cardiac ac celeration and an increase in arteriolar tonus Decreased blood flow in the medulla oblongata and possibly else where in the brain promotes increased vasoconstrictor tonus The rise in venous pressure elicits the Bainbridge cardiovascular reflex Ventricular filling is improved by the rise in venous pressure and through Starling s law more forcible contractions are stimulated Thus the extent of fall *in arterial pressure which tends to be produced by a given* degree of impairment of left ventricular action is not as great as it would be in the absence of these compensatory mechanisms It should be noted that the vasoconstriction which is elicited by a fall in blood pressure while serving to oppose the fall in arterial blood pressure contributes to further transfer of blood into the large veins of the sys temic and pulmonary circuits and thus favors a further rise in venous pressure

In summary the immediate effect of a decrease in cardiac output is a fall in arterial blood pressure and a rise in venous pressure The rise in venous pressure occurs because outflow of blood from the arterial tree exceeds input for a brief period until a new equilibrium is estab lished with a greater volume of blood in the large veins of both circuits In the second place a further increment in central venous pressure is produced by the transfer of blood into the veins incident to reflex vasoconstriction which is elicited from the fall in arterial blood pressure Reflex venoconstriction may be concerned temporarily in promoting a further rise in venous pressure (37) The rise in venous pressure has compensatory value in that it stimulates the heart so that the fall in cardiac output is not as great as it would be if the venous pressure were not elevated

At this point it may be re emphasized that the maximum increase in the volume of blood in the venous system that can be produced immediately following a decrease in cardiac output e g as seen from cardiac arrest or cardiac tamponade in the presence of a normal blood volume does not produce a rise in venous pressure as high as that seen in chronic congestive failure Blood redistribution is only one of several factors contributing to the rise in venous pressure in chronic failure Severe venous congestion incident to heart failure does not develop instantaneously and during the hours days or longer required for its de velopment the blood volume and interstitial fluid become elevated Since the rise in central venous pressure to the levels seen in chronic congestive heart failure appears to be dependent to a considerable degree upon an increase in the blood volume and an increased extravascular support the explanation for the rise in venous pressure resolves itself largely into an explanation for the rise in volume of the extracellular fluid (blood plasma and interstitial fluid)

RELATIONSHIP BETWEEN CARDIAC OUTPUT, RENAL BLOOD FLOW AND BLOOD VOLUME

The relationship between cardiac output and blood volume and the essential role of the kidney in this relationship has been discussed at length by Borst (10) In various conditions in which there is a decreased cardiac output the renal blood flow has been found to be disproportionately decreased This is true whether cardiac output is decreased because of a decreased venous return or because of heart failure (106 109 111, 132) Merrill (106) found in a series of 35 patients in whom the cardiac output was about 40% of normal that the renal blood flow was about 25% of normal Mokotoff *et al* (111) report an even greater decrease in renal blood flow Borst (10) has presented evidence that any decrease in cardiac output probably through changes in renal function caused by decreased renal blood flow leads to a reduction in the excretion of sodium chloride (and hence of water) so that the blood volume becomes elevated The increase in blood volume would serve to cause a rise in venous pressure which would be expected to stimulate the heart to a higher output Thus Borst views the retention of sodium chloride by the kidney in response to a decreased cardiac output as a homeostatic mechanism serving to restore the cardiac output The sequence of events postulated is summarized as follows



According to this view the rise in blood volume should be self limiting As the cardiac output approaches normal there is elimination of the basis for further retention of salt and the end result if the original cause for the de creased output persists is that a relatively normal output is attained through an elevated blood volume and venous pressure

McMichael has repeatedly emphasized the view that the rise in venous pressure in heart failure is a device for main taining a cardiac output within the normal range (97 99)

The recognition of the fact that renal function of a patient in congestive heart failure is different from the normal subject has stimulated many recent studies Some important results of these studies will be discussed later

Merrill and Stead and Warren contrary to Borst believe that the decreased sodium excretion associated with de creased renal blood flow should be viewed as being on the basis of impairment of renal function rather than as a homeostatic mechanism It appears that the choice of terms to apply to the phenomenon of sodium retention is de termined by the difference in views concerning the value of the concomitant rise in blood volume and venous pres sure rather than by any difference in viewpoint regarding the actual renal mechanisms involved The latter workers are less impressed than McMichael and Borst by the compensatory value of a mild or moderate rise in venous pressure and are more impressed with the difficulties en countered when the rise in venous pressure is excessive

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FAILURE OF THE VENOUS RETURN

REDUCED BLOOD VOLUME

When the blood volume is reduced compensatory mechanisms are brought into activity which help to maintain adequate flow of blood to vital organs Other mechanisms which act more slowly serve to restore the normal blood volume

Maintenance of Blood Flow in the Presence of Lowered Blood Volume The principal immediate responses to a sudden considerable decrease in blood volume e g from hemorrhage are shown in Figure 7 Loss of blood results in a fall in both arterial and venous pressure and each of these changes elicits compensatory responses The fall in arterial blood pressure is opposed by nervous and humoral mechanisms The falling pressure in the carotid sinuses and aortic arch results in reflex cardiac acceleration reflex vasoconstriction, and probably venoconstriction The vasoconstriction is accomplished on the efferent side largely through the activation of adrenergic nerves and is supplemented by reflex liberation of epinephrine The vasoconstriction helps to restore arterial blood pressure by impeding the outflow from the arterial tree and by promoting the transfer of blood into the venous system from blood reservoirs, tends to restore venous pressure The combination of rapid heart rate and low venous pressure results in a low difference between systolic and diastolic pressure i e pulse pressure is decreased. The left side of the diagram indicates a humoral mechanism for production of vasoconstriction in the presence of a chronically lowered blood volume The decreased renal blood flow is associated

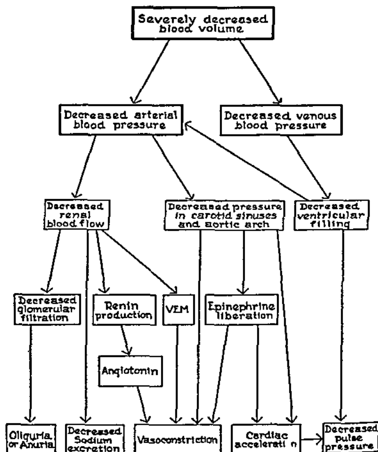


Figure 7 Mechanisms concerned with development of the typical cardio vascular pattern seen when the blood volume is severely decreased

with production of renin an enzyme acting upon a constituent of normal blood plasma to produce angiotonin a vasoconstrictor substance (34 60 76 120) The neural vasoconstrictor mechanism is elicited immediately whereas the humoral mechanism is more sluggish However the angiotonin mechanism appears to be suitable for maintenance of a more sustained vasoconstriction and in some

degree replaces the reflex mechanism which is less suitable for prolonged function As discussed by Ogden (118) it appears that some other mechanism replaces the angiotonin mechanism when there is a prolonged decrease in renal blood flow

According to the work of Chambers and Shorr and others (24 153) when the kidney is subjected to deficient circulation by various methods it produces a vaso-excitor material (VEM) which increases the sensitivity of arterioles to the constrictor action of epinephrine This substance may be concerned in part with the compensatory vasocon striction in shock However in later stages of shock a vasodilator material (VDM) is said to enter the circulation in progressively increasing amounts possibly contributing to production of irreversible shock

In a discussion of measurements obtained from patients suffering from *traumatic* shock Richards (132) states the essential finding in all appeared to be an inadequate venous return of blood to the heart with diminished cardiac output The anatomical factor immediately re sponsible in most instances was a deficit in circulating blood volume The studies reported by Richards demon strate selectivity of the vasconstrictor response in shock the blood flow through the kidney being reduced in some cases to 1/10 or 1/20 of the normal value when the cardiac output was reduced to one half the normal level The great fall in renal blood flow is interpreted as indicating that re sistance to blood flow through the kidney is dispropor tionately increased by severe constriction of the renal arterioles Since a relatively large part of the cardiac out put goes through the kidneys the advantage to other organs of a temporarily lowered renal blood flow in shock is clear However oliguria or anuria results and finally there is damage to the renal tubules if ischemia is pro longed

There are also *central mechanisms* for production of vasoconstriction in the presence of a decreased blood volume As blood flow through the medulla oblongata decreases the carbon dioxide tension in the medulla increases and this stimulates the *vasoconstrictor center*

When the blood volume has been severely decreased for a more or less prolonged period the arterioles apparently lose their ability to remain contracted in response to the usual stimulating agents A loss of arteriolar tonus will cause a decrease in venous return even in the presence of a normal blood volume and the deleterious effects of arteriolar relaxation are greater in the presence of a lowered blood volume When this stage is reached transfusions are relatively ineffective in increasing blood pressure since the blood pools in the capillary beds The reader can refer to Wiggers (196) for a detailed discussion of vasomotor reactions in the various stages of shock

Restoration of Blood Volume In the presence of a decrease in blood volume the decrease in hydrostatic pressure in the capillaries which is secondary to decreased volume and arteriolar constriction promotes transfer of fluid from the interstitial space into the blood stream Thus the fall in blood volume is counteracted at the expense of the interstitial fluid To a lesser degree intracellular fluid passes into the interstitial space The transfer of fluid into the blood from the interstitial space is reflected in a rapid decrease in the volume of red blood cells per unit of blood (hematocrit) The bone marrow is stimulated probably by lowered oxygen tension gradually restoring the hematocrit to normal

Physiological Rationale for Treatment The treatment in the syndrome of inadequate blood volume is directed at restoration of the venous return so that cardiac filling and hence cardiac output may be improved It consists firstly of measures which will assist venous return until

the blood volume can be restored and secondly of ad ministration of blood or blood substitutes Even though physiological saline solution is lost from the circulation following intravenous injection it may be valuable for maintaining circulation for a short period until blood or plasma is available The flow of blood to the heart may be improved by elevation of the foot of the bed This results in an increased central venous pressure and consequently an increased cardiac output Vasoconstrictor compounds have not proved to be of much value in the treatment of this syndrome In the reversible stage there is already severe vasoconstriction produced by the compensatory mechanisms described above In the later stages the arterioles fail to maintain their tonus in response to either the nervous or humoral mechanisms and therefore would be expected to be relatively unresponsive to pharmacologic vasoconstrictor agents

Finally a positive salt and water balance also would be expected to occur through the mechanisms diagrammed in Figure 7 and this would assist in restoration of normal volumes in the fluid compartments

LOSS OF ARTERIOLAR TONUS

The tonus of the smooth muscle in the arteriolar wall is under the influence of vasconstrictor and to a lesser degree vasodilator nerves These nerves constitute the final common path for various reflexes that influence ar teriolar tonus for central effects related to changes in blood composition (especially in CO_2 and pH) and for psychic effects Most of the vasoconstrictor nerves are adrenergic i e exert their action on arteriolar smooth muscle through the liberation of epinephrine or an epinephrine like substance A widespread inhibition of arteriolar tonus usually associated with a decrease in heart

rate may be produced on a reflex basis by massaging the carotid sinus Neurogenic vasodilatation commonly is associated with emotions Loss of arteriolar tonus may be produced by injection of vasodilator compounds such as doryl (carbaminoyl choline) or urecholine (carbaminoyl beta methyl choline) or by administration of agents like Dibenamine (dibenzyl beta chloroethylamine) which block the action of the adrenergic vasoconstrictor nerves

One of the primary physiologic functions of the vaso constrictor nerves is to prevent pooling of blood in the portion of the body below the level of the heart Therefore these nerves are particularly important in man in the standing position When a subject is in the reclining position there is only a mild degree of tonic i e continuous activity of the vasoconstrictor nerves This is evident from the effects on blood pressure and heart rate following administration of an adrenergic blocking agent such as Dibenamine While the subject is supine there is usually either no change in blood pressure or a slight decrease and typically there is a slight increase in heart rate The effects of the drug appear negligible until the patient stands then the blood pressure drops precipitously due to pooling in the dependant part of the body The adrenergic cardioaccelerator innervation is not blocked by Dibenamine and the heart is reflexly accelerated as a result of the fall in pressure in the carotid sinuses and aortic arch Under normal conditions when an individual changes from the supine to the upright position reflex activation of the vasoconstrictor pathways is elicited by the rise in pressure in the splanchnic vascular bed (68) and by any fall in pressure in the carotid sinuses and aortic arch There is also reflex cardiac acceleration from the latter receptors In the patient under the influence of Dibenamine the efferent pathways are activated following changes in blood pres

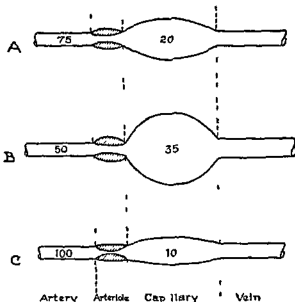


FIGURE 8 *Effects of alterations in arteriolar tonus upon pressure and volume in the capillaries* The figures are arbitrary and serve only to show direction of change

A Normal conditions

B As the arterioles relax the arterial pressure decreases and the pressure in the capillaries increases. A slight increase in pressure in the capillaries is associated with a large increase in volume

C Rise in arterial pressure and decrease in capillary pressure resulting from arteriolar constriction

sure but the chemical mediator produced at the adrenergic vasoconstrictor nerve endings is incapable of causing contraction of the smooth muscle in the arterioles thus allowing the blood to enter the distensible capillaries under an increased head of pressure The effects of changes in arteriolar tonus upon pressure and volume in the capillaries is shown graphically in Figure 8 If the patient remains in the upright position he may faint as a result of inadequate cerebral circulation If the patient is re

turned to the horizontal position circulation quickly returns to normal

The relation of activity of skeletal musculature to venous return becomes obvious in a patient who has received a large dose of an adrenergic blocking agent The patient may faint within one or two minutes after assuming the upright position if he stands still but if he walks circulation may be maintained Also circulation may be maintained if a tight abdominal binder is applied A circulatory syndrome similar to that produced by Dibenamine occurs spontaneously or idiopathically in some individuals and is known as orthostatic hypotension

The compensatory responses initiated by a sudden generalized loss of arteriolar tonus are similar to those which are initiated by a decrease in blood volume This is true because in each case there is a fall in both arterial and venous pressure and most of the compensatory reactions are secondary to these two changes Renal blood flow is *disproportionately decreased when there is generalized loss* of arteriolar tonus since other vascular beds normally offering higher resistance to blood flow are opened Under these conditions it is probable that there is a decreased excretion of salt The most prominent manifestations of a *chronic* decrease in arteriolar tonus (or more generally of a decreased resistance in the systemic circuit) are increased blood volume and increased cardiac output The mechanisms concerned with production of these changes are discussed on pages 23ff

OBSTRUCTION OF VENOUS DRAINAGE

Obstruction of a large systemic vein produces hemodynamic changes similar to those produced by loss of blood or by generalized vasodilatation Pressure upstream from the obstruction approaches arterial pressure and the blood

trapped in the capillaries and veins is not available for circulation The venous return to the heart decreases venous pressure and hence cardiac output and arterial pressure decrease These effects may be demonstrated by clamping the portal vein As blood continues to flow into the splanchnic vascular bed and cannot flow out the circulating blood volume decreases Venous pressure decreases cardiac output and arterial blood pressure decrease precipitously and cardiovascular compensatory reflexes are initiated

When one breathes into a bag containing gases under a pressure greater than atmospheric pressure there is partial obstruction to the entire systemic venous drainage plus an increased resistance to flow of blood through the pulmonary circuit (4 30) Barach *et al* (4) state The blood merely accumulates in the great veins until the pressure inside them is high enough to overcome the added external pressure The circulation is maintained at a higher level of intra auricular pressure but cardiac filling is at best not increased and may be decreased The rise in venous pressure is aided by two other processes (1) The displacement of blood from the lungs increasing correspondingly the volume of blood in the systemic circulation and (2) increased tone of the arteries and/or veins in the legs The increased resistance to flow of blood through the lungs is overcome by an increased strength of contraction of the right ventricle so that an output near normal is maintained

— 3 —

FAILURE OF THE HEART

ACUTE COMBINED RIGHT AND LEFT VENTRICULAR FAILURE

THE most extreme examples of simultaneous acute failure of the pumping action of both ventricles are cardiac standstill and ventricular fibrillation In each case pumping action of both ventricles suddenly ceases and there is no longer a basis for maintaining the pressure gradients in either the systemic or pulmonary circuits Blood volume and pressure decrease precipitously in the systemic arteries and increase in the systemic and pulmonary veins and in the atria Shortly pressure is equal throughout the circulatory system at the relatively low static pressure level

If the pumping action of both ventricles is decreased e g by toxic action of certain drugs on the myocardium or by an excessively fast heart rate resulting in a sudden decrease in cardiac output of a degree compatible with life both immediate and delayed adjustments occur The immediate adjustments elicited by decreased cardiac output are those already described on pages 17ff Another adjustment which becomes obvious only after a latent period is the increase in blood volume For example a patient may show evidences of an acute decrease in cardiac output at the onset of an attack of paroxysmal auricular tachycardia but does not have obvious venous congestion Venous congestion may develop if the attack persists for hours or days and during this period the blood volume becomes elevated (10) The rise in blood volume may be too rapid to be attributed to increased activity of the blood forming organs

but can be explained readily on the basis of retention of salt and water by the kidney

ACUTE FAILURE OF THE LEFT VENTRICLE

The chain of events seen in acute left ventricular failure stems from the decrease in left ventricular output The decrease in output results in a decrease in the pressure and volume of blood in the arterial tree and this in turn results in the changes diagrammed under decreased arterial blood pressure in Figure 7 In fact the pattern in the systemic arterial tree in acute left ventricular failure is not unlike that in hemorrhagic shock on the other hand unlike shock the central venous pressure and volume of blood in the pulmonary circuit is not decreased Typically it is increased Systemic arteriolar constriction is elicited by both humoral and nervous mechanisms the humoral mechanisms being activated largely by the disproportionately great decrease in renal blood flow (106 107 112) If cardiac output remains low the blood volume becomes elevated as the characteristic syndrome of chronic left ventricular failure develops

The differences between acute left ventricular failure and acute combined right and left ventricular failure (when not superimposed on chronic failure) are not striking In the former case the right ventricle is responding more normally to its venous return than the left ventricle so that the fraction of the total blood volume which is contained in the pulmonary circuit will be increased The pulmonary venous pressure will be elevated and the systemic venous pressure will be within the upper limits of the normal range or mildly elevated

CHRONIC FAILURE OF THE LEFT VENTRICLE

If the left ventricular output is chronically lowered and a rise in blood volume occurs both pulmonary and systemic venous pressure may be expected to rise further

following any further decline in left ventricular output so that the systemic venous pressure is elevated even though the right ventricle is capable of responding normally to the venous pressure In this circumstance the right ventricle is responding to the elevated systemic venous pressure with a more forcible contraction which serves to maintain flow through the pulmonary circuit into the left atrium in spite of the elevated pressure The left ventricle which is in failure in turn may respond to the elevated pulmonary venous pressure with a near normal output

RIGHT VENTRICULAR FAILURE IN THE PRESENCE OF LEFT VENTRICULAR FAILURE

Whenever the right ventricle fails subsequent to left ventricular failure a rise in systemic venous pressure is to be expected pulmonary venous pressure may decrease for a time but will remain above the normal level The mechanism is considered to be as follows As stated above the output of the left ventricle in failure is being maintained through the stimulus of elevated pulmonary venous pressure for which the right ventricle is responsible When the right ventricle fails the filling pressure for the left ventricle decreases and cardiac output falls With a fall in pressure in the systemic arterial tree there is also a fall in volume this volume being transferred to the systemic veins and thus producing a further elevation in systemic venous pressure If the systemic veins are only moderately filled as in acute left ventricular failure the transfer of blood associated with failure of the right ventricle will produce less of a rise in pressure than when it fails in the presence of chronic left ventricular failure In the latter case elevated blood volume as well as redistribution of blood is contributing to venous engorgement and further redistribution toward the venous side incident to

further decrease in left ventricular output would be expected to produce a considerable rise in venous pressure

ACUTE FAILURE OF THE RIGHT VENTRICLE

Experimentally acute and chronic impairment of the pumping action of the right ventricle has been produced by destruction of the tricuspid valves (90) by occlusion of all the major arteries supplying the right ventricle (70 162) and by cauterizing the right ventricular musculature (162) In acute experiments the right ventricle has been completely by passed for short periods by methods which also impair the coronary circulation (139 189) Such procedures when the remainder of the cardiovascular system is normal are compatible with the life of the animal The venous pressure is within normal limits or mildly elevated These results are not difficult to understand when the pressures in the various parts of the cardiovascular system illustrated in Figure 4 are considered The mean pressure in the pulmonary artery under normal conditions is only 15 17 mm Hg and a central venous pressure around 20 cm of water would be sufficient to maintain blood flow through the lungs in the absence of any pumping action of the right ventricle

CHRONIC FAILURE OF THE RIGHT VENTRICLE

In chronic weakness of the right ventricle as the only defect in the cardiovascular system one would expect that the systemic venous pressure might become elevated to a level sufficient to perfuse the lungs This rise in venous pressure would be produced by the mechanisms elicited by decreased left ventricular output The level reached would not need to be as high as that commonly seen in chronic congestive heart failure with edema and one would not expect that severe chronic congestive heart failure would develop even

though the right ventricle be non functioning as a pumping chamber

Chronic experiments which serve to clarify this problem include destruction of the tricuspid valve (90) which permits the right ventricle to pump a large portion of its contents back into the systemic venous system and infarction of the right ventricular musculature by ligation of the *arteries carrying its blood supply (70 162) Dogs may* recover from these surgical procedures and live for a prolonged period without developing venous congestion *Al*though it may be objected that in these experiments the pumping action of the right ventricle has not been completely eliminated it does seem likely that complete inactivation of the right ventricle when the left ventricle is intact and resistance in the pulmonary circuit is normal would not result in venous congestion of the degree commonly seen in chronic congestive heart failure

Now the background has been established for discussion of true chronic congestive heart failure as an entity The cardiovascular adjustments will be described basic causes will be classified and the mechanism of the rise in blood volume will be discussed

TRUE CHRONIC CONGESTIVE HEART FAILURE

Cardiovascular Adjustments In chronic congestive heart failure there is an increase in the amount of blood and in pressure in the great veins As failure progresses there is a gain in weight disproportionate to the caloric intake and eventually there may be edema in the lungs or in the dependant parts of the body or both The lesions which lead to chronic congestive heart failure are present prior to the development of the characteristic features of the syndrome The pathologic physiology of this precongestive phase has been the subject of numerous investigations and the following facts have been demonstrated The degree

of increase in the cardiac output in response to a stand ard exercise test is less than normal (2 69 97 109 114) the time required for the oxygen consumption to return to the basal level is longer than normal (114) and the increase in cardiac output which is elicited by increasing the venous pressure as by venous infusions or by changes in posture is less than normal (97) At this early stage the cardiac out put under basal conditions may be within the normal range on the other hand the output does not increase under stress to the levels which are attained in normal subjects An increase in the venous pressure when the patient is at rest occurs at a relatively advanced stage in the development of congestive heart failure Even at this *stage the cardiac output may be within the normal range* for the oxygen requirement of the patient the decompen sated heart is maintaining a normal output in the presence of and possibly in response to an elevated venous pressure (97) As the decompensation becomes more severe the venous pressure becomes further elevated and a stage is finally reached in which the cardiac output is considerably reduced even though the venous pressure is quite elevated In the most severe forms the venous pressure is elevated to the point of overdistending the ventricle so that cardiac output actually may be reduced as a consequence of the excessive venous pressure (99) From these facts it would seem that in both the pre-congestive and the congestive phase a failing ventricle is one which does not respond to a given venous pressure with an output as great as that of the normal ventricle The pressure-output curve is displaced downward as illustrated in Figure 2

An increase in blood volume is a consistent finding in chronic congestive heart failure except in certain stages in which the venous pressure may be maintained through increased extra vascular support of the walls of the veins (123) Increased venous pressure is brought about in part

through the increase in blood volume and these changes in blood volume and venous pressure may be viewed as compensatory in that the heart is stimulated to maintain a normal or more nearly normal output

In short there are three prominent and reasonably consistent basic findings in true chronic congestive heart failure as defined above 1) subnormal increase in cardiac output in response to a given increase in venous pressure 2) elevated venous pressure and 3) increased blood volume The increased blood volume in the presence of a sustained arteriolar tonus contributes to the elevation of the venous pressure and this in turn may stimulate the heart to maintain an output within the normal range with the patient at rest During exercise the output typically does not increase to the extent that it increases in normal subjects

Basic Causes If chronic congestive heart failure is to include by definition only those cases in which there is impairment of transfer of blood and since the transfer in the final analysis is dependent on the left ventricle the causes of chronic congestive heart failure may be classified under three headings 1) Hypodynamic left ventricle 2) Interference with filling of the left ventricle and 3) Inefficient left ventricle

The left ventricle may be hypodynamic that is lack the force to pump blood because of 1) involvement of the left ventricular musculature from infarction fibrosis deficiency of metabolites toxins etc and 2) excessively fast rates etc The mechanisms for elevation of venous pressure in such cases are as already described for a sustained decrease in left ventricular output i e there is redistribution of blood toward the venous side and a more or less gradual increase in blood volume Output may approach normal through the stimulation of the left ventricle by an elevated pressure in the pulmonary circuit or it may be low even though the venous pressure is elevated or when the filling

pressure is excessive the overdistention of the ventricle may cause a further decrease in output In the latter case it is possible that improved cardiac output may be obtained by venesection but in cases in which this level of pressure has not been reached venesection would be expected to cause a decrease in cardiac output In chronic congestive failure occurring because of a hypodynamic left ventricle both pulmonary and systemic venous pressure may be elevated but the rise in pulmonary venous pressure is greater since the left ventricular output is maintained at the level of the right ventricular output only when the left ventricle fills under a higher head of pressure When the right ventricle fails subsequent to chronic left ventricular failure as a consequence of chronic changes incident to pumping against an elevated pressure pressure in the pulmonary circuit falls therefore left ventricular filling and consequently left ventricular output decreases and there is a further increase in systemic venous pressure

In summary a hypodynamic left ventricle will cause an increase in volume and an increase in pressure in the pulmonary circuit and in the systemic veins but the engorgement is more prominent in the pulmonary vascular bed When the right ventricle fails also a fall in pulmonary pressure and in left ventricular output results and there is a further rise in systemic venous pressure

There are a number of lesions which may be grouped together in that they *interfere with left ventricular filling* so that a normal or subnormal filling occurs in the presence of an elevated venous pressure These may be subdivided into those characterized by 1) Obstruction to flow of blood or backflow at the tricuspid valve 2) Obstruction to the flow of blood at the pulmonic valve or in the pulmonary circuit or at the mitral valve typically combined with failure of the right ventricle and 3) Interference with left ventricular filling by compression of the heart

from without The hemodynamics must be considered separately in each of these three types

1 In tricuspid stenosis or insufficiency the filling or the output of the right ventricle is maintained through an elevated venous pressure The rise in venous pressure may be visualized as occurring as follows As the stenosis develops *it would tend to decrease right ventricular filling consequently left ventricular filling and output* would not be maintained Decreased left ventricular output would result in increased venous pressure by the mechanisms already described The rise in systemic venous pressure would tend to restore right ventricular filling to normal In tricuspid insufficiency an increased filling incident to an elevated venous pressure results in an increased stroke volume through Starling s law so that the net output of the right ventricle is maintained even though some of the blood is pumped back through the tricuspid valve Therefore a normal flow of blood to the left ventricle is maintained

2 When there is obstruction to flow of blood in the pulmonary circuit or at the mitral valve the right ventricle through Starling s law responds to the increased resistance to outflow with increased strength of contraction and may maintain a normal output and hence normal filling of the left ventricle This is analogous to the maintenance of a normal output by the left ventricle against greatly elevated systemic arterial blood pressure If the right ventricle fails then left ventricular filling and output are not maintained When this occurs the venous pressure rises as in any case where left ventricular output decreases

3 In cardiac compression a situation is encountered in which there is elevated venous pressure serving to maintain normal or even subnormal filling Stroke volume is low and the tendency for the output and arterial blood pres-

sure to fall is opposed by reflex cardiac acceleration As the condition becomes more severe the left ventricular output is not maintained and consequently the venous pressure rises

The left ventricle may be said to be inefficient in those conditions in which it must re pump blood i e mitral or aortic regurgitation In either case the net output is less than *the actual left ventricular output* Refilling from the aorta during diastole will through Starling s law stimulate a stronger contraction which may compensate for the amount of blood which regurgitates If left ventricular output is not maintained venous pressure will become elevated by the mechanisms already described In mitral insufficiency the net left ventricular output tends to be re duced with the consequent rise in venous pressure and restoration of a near normal output

Blood Volume An increase in venous pressure is an integral part of the syndrome of chronic congestive heart failure In an elastic system an increase in pressure is pro duced when the holding capacity of the system is de creased or when the fluid content is increased Active arte riolar constriction and venoconstriction are possible mecha nisms for decreasing the holding capacity of the cardiovascu lar system Normally the venous system is only partially filled with blood and a considerable decrease in holding capacity of the cardiovascular system incident to contraction of smooth muscle in the vascular tree promotes filling of the large veins but does not cause an increase in venous pres sure of the magnitude seen in congestive failure It is true however that after the extra-cellular fluid has reached high levels in chronic congestive failure there may be enough additional extra vascular support to maintain a high venous pressure with little increase in intra vascular volume (159)

It seems as Starr has said (162) that the simplest ex planation for the increase in venous pressure is that it

is produced in considerable part by an increase in blood volume Many investigators have measured the blood volume in patients with congestive failure Altschule (2) summarized the work in this field prior to 1938 and found general agreement that there is a significant rise in blood volume during the course of chronic congestive heart failure Gibson and Evans (55) showed an increased blood volume and demonstrated a direct correlation between the degree of increase in blood volume and the severity of the symptoms Seymour Pritchard Langley and Hayman (150) found an average increase of 25% in blood volume The majority of the measurements have been made using the dye methods particularly Evans blue Various objections to the dye methods recently have been discussed by Peters (123) and by Nylin and Hedlund (117) Starr s studies concerning the venous pressure in patients with and without congestive failure both in life and after death were described on page 14 The increase in the static blood pressure is presumptive evidence of an increased blood volume Several investigators (116 125 148 172) using the carbon monoxide method have found a significant increase in blood volume during decompensation The blood volume was decreased following digitalization Nylin (116) and Nylin and Hedlund (117) in measuring the erythrocyte volume and the whole blood volume by means of radioactive phosphorus found that both were increased during decompensation As compensation was restored the blood volume fell 28% and the erythrocyte volume fell 18%

It has been suggested repeatedly that the peripheral hypoxia which is found in congestive failure stimulates production of erythrocytes the blood volume increasing secondarily However oxygen lack does not cause as rapid or as great an increase in blood volume as occurs in some cases of congestive failure Moreover in the early stages

of failure the change is in the direction of hemodilution rather than hemoconcentration (122 150 178) However it is possible that hypoxia is concerned with stimulating the bone marrow to maintain the hematocrit at normal levels in the presence of a chronic increase in plasma volume The information available at present indicates that the rise in blood volume in patients with true chronic congestive failure is related to retention of salt and hence of water by the kidney secondary to reduced renal blood flow

Changes in renal function in patients with heart failure are summarized below

1 *Renal blood flow* as determined by para amino-hippurate clearance is markedly reduced in the patients with congestive failure who have a significantly decreased cardiac output (106 109 111 150 183) Moreover the per cent reduction in renal blood flow greatly exceeds the per cent reduction in cardiac output (106 111)

2 *Glomerular filtration* as shown by inulin or mannitol clearance is decreased in patients having a decreased cardiac output but it is not decreased as markedly as renal blood flow i e the filtration fraction is increased Mokotoff Ross and Leiter (111) in 16 patients found a filtration fraction twice normal in the presence of a renal blood flow of one third normal

3 *Urinary sodium excretion* is decreased Futcher and and Schroeder (52) determined the increase in sodium excretion after adding a given amount to the basal intake and found that in patients with congestive failure it was less than 30% of normal Reaser and Burch (129) using radioactive sodium reported that a normal control subject excreted ninety times as much sodium as a decompensating patient on the same salt intake Threefoot Gibbons and Burch (181) showed that patients while decompensating excreted less sodium than the controls and while recom

pensating excreted more sodium than the controls Numerous other papers in which a reduced sodium excretion has been found in patients with congestive failure are indicated in the key to the bibliography

4 *Tubular reabsorption of sodium* is not impaired It is normal or increased Mokotoff (111) found that the mean tubular reabsorption was the same per 100 cc of glomerular filtrate in patients with or without heart failure Other investigators maintain that under certain conditions sodium absorption is increased

5 *Water excretion* as measured by the diuretic response to drinking water is relatively unimpaired On a dietary salt intake of one gram per day water diuresis occurs as completely in the cardiac as in the normal subject Adequate studies have been made by Schemm (145 146) and many others (17 57 88 89 147 194) showing the importance of restricting salt and the advantages of allowing fluids *ad lib* in patients with congestive heart failure

The alterations in renal function described above show *no correlation with the venous pressure per se* However there seems to be a definite correlation with the adequacy of the cardiac output Whenever the cardiac output drops below that which is required to satisfy the metabolic needs of the body there is an immediate change in renal functions The primary change in renal function incident to decreased renal blood flow is the retention of sodium and secondarily the retention of water This tends to increase the intravascular and interstitial fluid volume and therefore venous pressure An elevated venous pressure will cause increased filling of the ventricle and consequently through Starling s law will tend to restore cardiac output to the normal range During this stage as mentioned by *Peters (123) a transfusion may help to restore a normal* output and phlebotomy may cause an acute decrease in output Renal retention of salt and water is only one of

several mechanisms which are operating simultaneously at least in the acute stages all tending to maintain cardiac output

The demonstration of a decrease in renal blood flow and an increase in the filtration fraction in patients with congestive failure points toward constriction of the efferent arterioles of the kidney (106) This constriction appears to be independent of the nervous pathways to the kidney (112 183) and perhaps is caused by the same humoral mechanisms which help to maintain the continued general arteriolar constriction characteristic of chronic congestive failure A search is under way for the humoral basis for the changes Merrill (110) has found renin in the renal vein of patients in failure suggesting angiotonin as a mediator of the arteriolar constriction A role of adrenal steroid hormones has been suggested and it is known that over dosage with desoxycorticosterone will produce the clinical picture of congestive heart failure (50 95 179) Further work is necessary before the exact mechanisms by means of which an insufficient cardiac output causes renal retention of salt and water can be described A detailed hypothesis has been presented by Wesson Anslow and Smith (193)

— 4 —

CHRONIC VENOUS CONGESTION WITHOUT HEART FAILURE

DIFFERENTIATION FROM TRUE CONGESTIVE HEART FAILURE

IN PRECEDING sections we have described the development of venous congestion following more or less obvious defects in or interference with the transport of blood in the cardiovascular system In these conditions the cardiac output is either *normal* or *decreased* when considered in relation to the oxygen consumption

There are other chronic conditions in which venous pressure and blood volume are elevated the heart is enlarged and edema may develop yet the cardiac output is *elevated* above the normal range The best example of this combination of findings is seen in the early and intermediate stages of beriberi There is a similar picture but to a lesser degree in some cases of systemic arteriovenous fistula These conditions are not related to interference with the transport of blood in fact the resistance to flow in the systemic circuit is decreased in each case Also in hyperthyroidism cardiac output may be above the range for normals but is not increased when considered in relation to the oxygen requirement When true heart failure occurs in hyperthyroid patients as in any case of failure the venous pressure is elevated and the ratio of cardiac output to oxygen consumption is normal or decreased

Attempts to discuss the pathologic physiology of the conditions not associated with defective transport of blood in the same category with conditions which are character

ized by defective transport lead to confusion concerning the mechanisms involved in congestive heart failure The initial change in the cardiovascular system differs in the two groups of conditions *in true congestive failure defective transport leads to increased blood volume in the other group increased blood volume occurs on some basis other than defective transport, and the heart is stimulated to a higher than normal output* The latter syndrome may be called chronic venous congestion without failure If chronic venous congestion becomes sufficiently severe then a decrease in cardiac output may occur from over distention of the ventricles

The difference between these two syndromes both as to basic mechanisms concerned and efficacy of methods of treatment is generally recognized and a subdivision into these two categories is commonly made tacitly if not actually For example Wood and Paulett (199) say Effect of digoxin on the venous pressure or right atrial pressure was measured in four cases of classical congestive heart failure and in 12 with venous pressure raised for other reasons In the four examples of congestive heart failure the venous pressure or right auricular pressure fell conspicuously within 30 minutes and the cardiac output when measured rose In the twelve patients without congestive heart failure the right auricular pressure did not alter appreciably within 40 minutes The cardiac output when measured was either unchanged or fell with the pulse rate

Chronic venous congestion without failure includes by the above definition all conditions in which venous congestion is secondary to an increase in blood volume occurring on a basis other than a defect in the transport of blood In these conditions the arteriolar tonus is sustained well enough so that the excess volume is contained largely in

the venous system and cardiac chambers rather than in the systemic capillary bed Such conditions should not be re ferred to as heart failure since there is no weakness of the heart demonstrable by the tests we now have (160) The heart is responding with increased output and increased work as a normal heart would be expected to respond under the same stimuli

EXAMPLES OF THE SYNDROME

Chronic venous congestion without failure definitely occurs in certain stages of beriberi and apparently occurs in some cases with arteriovenous fistula possibly it may occur in certain stages of desoxycorticosterone overdosage in patients with adrenal cortical insufficiency Experimen tally venous congestion can be produced by excessive blood transfusion alone or by transfusion plus adminis tration of vasoconstrictor compounds or in some species by overdosage with vasoconstrictor compounds in the pres ence of a normal blood volume When the rise in venous pressure incident to the rise in volume in the venous system is mild or moderate venous congestion without failure is produced but when the venous pressure is ele vated excessively the ventricles become overdistended so that cardiac output decreases When a decrease in cardiac output occurs as a result of severe venous congestion further flow of blood to the venous side would occur as arterial pressure decreases and the deleterious effects of this transfer would be great since the venous system is already overfilled

Various diseases and some methods of management of patients lead to an increase in blood volume and second arily to chronic venous congestion in the absence of car diac weakness At present it is not possible to list all of the diseases concerned or all of the mechanisms by means

of which the blood volume may become increased The hemodynamics in arteriovenous shunt and in beriberi will be described here briefly to introduce the problem and to compare and contrast this syndrome with true chronic congestive heart failure

Systemic Arteriovenous Fistula Arteriovenous fistula does not always lead to venous congestion and does not provide the best example of the syndrome but it is most instructive to consider it first since in this case there is a single and evident defect leading to the development of the final complex pattern of findings In arteriovenous fistula the resistance to flow of blood from arteries to veins is decreased in proportion to the size of the fistula All other deviations from normal must stem from this initial change In the one-circuit model illustrated in Figure 5 this situation may be simulated by opening the clamp which determines the resistance to flow from the arterial to the venous side If only this change is made the *pump output* and *fluid volume* remaining constant a certain volume of fluid is transferred from the arterial side to the venous side so that a new equilibrium is established at a higher level of venous pressure and a lower level of arterial pressure The rise in pressure on the venous side is considerably less than the fall on the arterial side since the venous side is relatively less filled and is more distensible However in the experimental animal when an arteriovenous fistula is opened not only is the peripheral resistance decreased as in the model there is also an increase in the volume of blood retained in the veins and capillary beds peripheral to the fistula This constitutes a decrease in the volume of blood returning to the right atrium and hence available for circulation Thus to simulate in the one circuit model the conditions on the arterial and venous side in an arteriovenous fistula it is necessary not only to

reduce the peripheral resistance but also to withdraw some blood from the system The reduction in volume will decrease or neutralize the rise in venous pressure incident to decreased peripheral resistance

The changes produced by opening and closing an arteriovenous fistula in man or experimental animals may

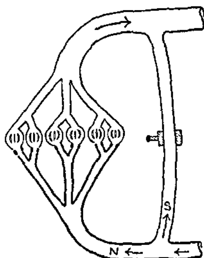


FIGURE 9 *Schema of a systemic arteriovenous fistula* Compare with Figure 3

N refers to the fraction of the cardiac output flowing through normal channels

S" refers to the fraction flowing through the shunt

be emphasized by considering the systemic blood flow in two parts S being that which flows through the shunt and N being that which flows through the normal channels This is illustrated in Figure 9 In the presence of a given head of pressure in the arterial tree N and S will be determined by the respective resistances in the two paths that the blood can take As the shunt is closed pressure in the entire arterial tree is elevated and flow in N is increased

When the shunt is opened the reverse occurs It is obvious that opening a large arteriovenous fistula will cause a decrease in the blood flow in the artery beyond the shunt it is also true that it will decrease the flow in the arteries which are not anatomically involved For example opening a large arteriovenous fistula e g between the iliac artery and vein will result in a decreased renal blood flow both by lowering the head of pressure in the renal artery and by eliciting reflex constriction of renal arterioles

Holman (71) lists as follows the changes produced by establishing an arteriovenous fistula in the experimental animal

The immediate changes due to the establishment of a fistula are

1 A fall in general arterial blood pressure affecting both systolic and diastolic levels

2 An increase in pulse rate

3 An increase in venous pressure proximal as well as distal to the fistula which is slight or pronounced according to the size of the fistula

4 An increase in cardiac output depending upon the size and location of the fistula

5 A very temporary decrease in the size of the heart and of the artery proximal to the fistula due to the sudden diversion of blood from the arterial into the capacious venous system an alteration comparable to that seen in massive hemorrhage

The more remote effects following the introduction of fistula are

1 A permanent diversion of part of the circulating blood from the normal capillary bed into the fistulous circuit

2 A gradually increasing total blood volume pro

ceeding *pari passu* with the amount of blood diverted through the fistula

3 A gradual dilatation of the heart and of the artery and vein proximal to the fistula due to the distending effect of an increased volume or bulk of blood attracted to the fistulous circuit because of its lessened resistance

4 The development of an extensive collateral circulation due to the lowered resistance to the flow of blood at the site of the fistula In the presence of a constriction of the artery proximal to the fistula a comparatively rare occurrence clinically this extensive collateral circulation pours blood into the artery distal to the fistula thus causing a dilatation of the artery to occur distal to the fistula instead of proximal to it

5 Slight hypertrophy of the heart due partly to dilatation and overdistention and partly to the increased work necessary to propel forward the increasing volume of blood flowing through it The enlargement of the heart is due mainly to a dilatation and only to a very minor degree to hypertrophy

6 A gradual recovery from the lowered blood pressure noted immediately after the formation of the fistula the systolic being equal or higher the diastolic definitely lower than that existing before the formation of the fistula thus producing a greatly increased pulse pressure

Holman s view of the problem and his recognition of the relationship between this and quite different causes of venous congestion are evident from these statements in his introduction A direct communication between the arterial and venous systems is a unique lesion that illus

trates as no other lesion can certain physiological con cepts of fundamental importance in the understanding of both the acquired and congenital disorders of the cir culatory system Under no other circumstances for example is it possible to produce such a startling increase in general blood pressure as may be produced by the simple expedi ent of closing a large peripheral fistula In seeking an explanation for this phenomenon it was necessary to in troduce a new concept namely an increase in the total volume of circulating blood as a compensatory reaction to the altered hydrodynamics of the circulation resulting from the fistula It is probable that this same concept of an increase in total blood volume is applicable in the ex planation of some of the circulatory phenomena attending such cardiac disorders as incompetent valves and congeni tal malformations

In the years since Holman s monograph it has become increasingly evident that various conditions resulting in a chronic decrease in renal blood flow promote an increase in the blood volume possibly through the retention of salt and as diagrammed in Figure 10 this is probably the mechanism for the increased blood volume in arterio venous fistula

The immediate compensatory mechanisms acting in arteriovenous shunt are mainly those which are associated with the decrease in arterial pressure Cardiac output is increased but apparently not to a level sufficient to restore capillary blood flow to normal Later blood volume in creases and it is probable that this serves as an additional stimulus through restoration or even elevation of right atrial pressure (26) to increase the cardiac output so that adequate capillary blood flow is maintained in spite of the loss across the shunt Holman (71) states that the extent of the increase in total blood volume depends upon the size

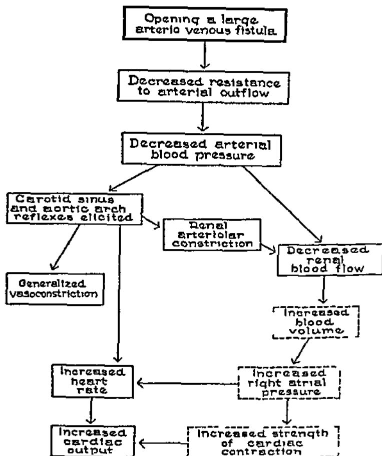


FIGURE 10 *Basis for development of the changes in the cardiovascular system following the opening of a large arteriovenous fistula* Acute adjustments are indicated in solid line boxes the more chronic changes in broken line boxes

of the fistula After operative removal of a large arteriovenous fistula there is typically a considerable decrease in blood volume amounting to as much as 1000 cc (41) per square meter of body surface

Beriberi A consistent pattern of cardiovascular changes

is seen in patients suffering from severe deficiency of thiamine (6 23 126) As in patients with true congestive failure there is increased heart size increased venous pressure increased blood volume and there may be edema Unlike the cases with true failure (defective transport of blood) the cardiac output is greatly elevated even when considered in relation to the oxygen consumption which is also elevated circulation time and arteriovenous oxygen difference are decreased rather than increased The abnormal cardiovascular pattern develops from thiamine deficiency and is slowly reversible when thiamine is administered

Porter and Downs (126) carefully studied the circulation in two patients with severe beriberi They state Our observations bear out those of others that during congestive heart failure associated with vitamin B deficiency there may be an increased cardiac output a low arteriovenous oxygen difference an elevated venous pressure and a shortened circulation time During recovery there is a change toward normal of these measurable circulatory phenomena viz a decline in cardiac output an increase in the arteriovenous oxygen difference a fall in venous pressure and a prolongation of the circulation time In addition in the one patient studied it was shown that during failure there was a marked increase in the plasma and total blood volume both of which returned to normal during recovery They further state We also found in both patients an initially high oxygen consumption which likewise gradually returned to normal under observation It may be argued that this high oxygen consumption accounted for the high cardiac output values but the fact that the arteriovenous difference was abnormally low indicates that the cardiac output was increased out of proportion to the metabolic needs of the body Roentgen rays of the heart shadow in both cases showed the dimensions

considerably increased beyond normal before therapy Beginning a few days after the start of therapy there was a progressive decrease in the size of the heart shadows which gradually returned to normal limits within two weeks The electrocardiograms in both patients revealed essentially normal complexes at the beginning of observation and no definite change following therapy The study by Burwell and Dexter (23) by newer techniques is in agreement with that of Porter and Downs (126) on essential points

In this syndrome as Starr has commented (23) the heart behaves as if it is stimulated rather than as if it is weak What then is the source of the stimulation? It is probable that a metabolic defect incident to chronic thiamine deficiency causes vasodilatation This would result in reflex cardiac stimulation Also in the presence of generalized vasodilatation the resistance to flow in the kidney where resistance is already low is not decreased as much as in other vascular beds This results in a decrease in renal blood flow until compensated by an increased cardiac output Thus one may speculate that in beriberi a decrease in renal blood flow may provide the basis for the rise in blood volume which would serve as a further stimulus to the heart

Weiss and Wilkins (192) state that arteriolar constriction following B_1 therapy must also react in turn centrally on the heart in the same beneficial manner as the closing of an arteriovenous aneurysm It is quite possible that the initial defect in the cardiovascular system in these two conditions is the same i e a decreased peripheral resistance and hence the sequence of events depicted in Figure 10 also may apply to beriberi On the other hand pathologic material indicates that the myocardium may be damaged in the later stages of beriberi In any case in either beriberi or arteriovenous shunt it is to be expected

that a decrease in cardiac output from the abnormally high level will develop if the blood volume and venous pressure become excessive so that the ventricles are over distended

An understanding of what has led to a rise in blood volume and chronic venous congestion in the individual case is necessary before the correct treatment can be instituted If the heart is weak and the cardiac output is normal or low the value of digitalis and related compounds as an adjunct to various other measures is well established If the heart is not weak and the output is high digitalis alone will be relatively ineffective or even detrimental specific therapy determined by the etiology of the disease is necessary along with other measures which influence the blood volume

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Sodium restriction 17 22 57 88 89 123 130 145 146 147 194

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and

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